

## LIST OF ABSTRACTS OF THIS ISSUE

### PREVENTION OF THROMBOEMBOLIC COMPLICATIONS IN PATIENTS WITH ATRIAL FIBRILLATION AFTER CORONARY ARTERY STENTING

**E.P. Panchenko, MD, Prof.**

Myasnikov Research Institute of Clinical Cardiology, Russian Cardiology Research and Production Complex, Russia's Ministry of Health, Moscow

**A**trial fibrillation is one of the most common cardiovascular diseases. In atrial fibrillation the incidence of systemic thromboembolism and stroke increases fivefold. Coronary artery stenting in coronary artery disease is another risk factor for thrombotic events. The article discusses the problem of anticoagulation therapy in patients with atrial fibrillation after coronary artery stenting.

### THE APPROPRIATENESS OF ANTITHROMBOTIC THERAPY IN NON-VALVULAR ATRIAL FIBRILLATION IN CLINICAL PRACTICE

**Baranova<sup>1,2</sup> E.I., Soboleva<sup>1,2</sup> A.V., Aznauryan<sup>1</sup> R.S., Ionin<sup>1</sup> V.A., Chubenko<sup>1,2</sup> E.A., Katsap<sup>1</sup> A.A., Yatsuk<sup>1,2</sup> D.I.**

<sup>1</sup> St. Petersburg State Medical University named after academician I.P. Pavlov, the Ministry of Health of the RF;

<sup>2</sup> Federal North-West Medical Research Centre, the Ministry of Health of the RF.

**A**im. To assess the risk of stroke and type of antithrombotic therapy at the outpatient and inpatient treatment stages in patients with non-valvular atrial fibrillation. Material and methods. 576 medical records of patients admitted to cardiology unit in 2013 were studied. Risk factors for stroke and systemic embolism were evaluated using the CHA2DS2-VASc score and antithrombotic therapy was considered. Results. Atrial fibrillation was diagnosed in 26.3% of patients. Non-valvular atrial fibrillation was diagnosed in 82.2% of those. 111 (88.8%) patients had a score of 2 or more on the CHA2DS2-VASc, 13 (10.4%) patients had a score of 1 and only 1 patient had a score of 0 points. The average CHA2DS2-VASc score in patients with

atrial fibrillation was  $3.9 \pm 1.0$ . Only 40% of patients with non-valvular atrial fibrillation received anticoagulants at prehospital stage. 38.4% of patients received antiplatelet agents and 21.6% of patients did not receive antithrombotic therapy. Only 26.8% of patients taking warfarin had target INR at admission. Anticoagulant therapy was prescribed to 93 outpatients (74.4%). Conclusions. A majority of patients with non-valvular atrial fibrillation who were hospitalized in the cardiology clinic had a high risk of stroke and systemic embolism, though they did not receive appropriate antithrombotic therapy. In patients with non-valvular atrial fibrillation, the risk of stroke should be assessed using the CHA2DS2-VASc score, and those at high risk should receive anticoagulant therapy.

**KEYWORDS:** atrial fibrillation, new direct oral anticoagulants, anticoagulant therapy.

### CARDIOVERSION USING RIVAROXABAN IN PATIENTS WITH NON-VALVULAR ATRIAL FIBRILLATION: RESULTS OF THE X-VERT STUDY

**Yavelov I.S.**

MD, leading researcher, SRI of Physical-Chemical Medicine, Federal Medical and Biological Agency of Russia, Moscow

**R**ecently, much attention has been given to the use of new oral anticoagulants (NOAC) for the prevention of thrombotic events in patients at high risk. The efficacy and safety of using NOAC registered in Russia is widely discussed today. In September 2014, the results of the X-VERT study investigating rivaroxaban were published. That was the first prospective, multicenter, randomized, open study into use of a NOAC in cardioversion in patients with atrial fibrillation. According to the X-VERT study, rivaroxaban appears to be an effective and safe alternative to vitamin K antagonists and may allow prompt cardioversion in hemodynamically stable patients with paroxysmal non-valvular atrial fibrillation.

**KEYWORDS:** cardioversion, non-valvular atrial fibrillation, X-VERT, rivaroxaban, thrombosis prophylaxis

## **EFFICACY AND SAFETY OF DABIGATRAN IN ELDERLY PATIENTS WITH NON-VALVULAR ATRIAL FIBRILLATION IN CLINICAL PRACTICE (RESULTS OF THE MEDICARE STUDY)**

**Vorobyova N. M., Panchenko E. P.**

Russian Cardiology Research and Production Complex,  
Russia's Ministry of Health, Moscow

**T**his review article tells about the results of the Medicare observational cohort study the purpose of which was to obtain more information on efficacy and safety of dabigatran in more than 130 thousand elderly (over 65 years) patients with non-valvular atrial fibrillation eligible for free medical care under the Medicare program (USA). The obtained results are consistent with the results of the previous studies — RE-LY and RELY-ABLE, and demonstrate higher efficacy of dabigatran in reducing risk of stroke, intracerebral hemorrhage and death compared to warfarin. However, dabigatran is characterized by less safety than warfarin, and associated with a higher risk of gastrointestinal bleeding.

**KEYWORDS:** atrial fibrillation, anticoagulant therapy, dabigatran

## **THROMBIN GENERATION TEST IN THE ESTIMATION OF EFFECTS OF ANTIPLATELET AGENTS IN PATIENTS WITH CORONARY HEART DISEASE AFTER PERCUTANEOUS CORONARY INTERVENTION**

**Berezovskaya<sup>1,3</sup> G.A., Smirnova<sup>2</sup> O.A.,  
Petrishchev<sup>1,3</sup> N.N., Papayan<sup>2</sup> L.P., Karpenko<sup>3</sup> M.A.,  
Golovina<sup>2</sup> O.G., Khromov-Borisov<sup>1</sup> N.N.**

<sup>1</sup> St. Petersburg State Medical University named after academician I.P. Pavlov, St. Petersburg;

<sup>2</sup> Russian Research Institute of Hematology and Blood Transfusion, FMBA of Russia, St. Petersburg;

<sup>3</sup> Federal North-West Medical Research Centre, the Ministry of Health of the RF

**A**im: To explore the possibilities of using thrombin generation test in platelet-rich and platelet-poor plasma to assess the impact of dual antiplatelet therapy in patients with CHD after percutaneous coronary intervention. Material and methods: The material for the study was venous blood of 54 patients with CHD aged 53

to 77 years after percutaneous coronary intervention with stent placing within a year and receiving clopidogrel and aspirin in standard doses (75 and 75-100 mg daily, respectively), and of 40 people comparable by age and sex, without clinical manifestations of CHD and not receiving the drugs for any other purpose. Thrombin generation test was performed in platelet-rich and platelet-poor plasma. Intravascular activation and induced platelet aggregation, as well as routine coagulation indicators, were evaluated. Results: Administration of antiplatelet agents did not affect the results of routine coagulation tests or intravascular platelet activation. The evaluation of induced platelet aggregation demonstrated that antiplatelet agents had the most significant impact on collagen-induced platelet aggregation ( $p = 10^{-7}$ ). The thrombogram showed that in platelet-rich plasma the most significant impact of antiaggregants was in a decrease in endogenous thrombin potential (ETP;  $P = 0,0045$ ) and peak thrombin concentration (PT;  $P = 4 \cdot 10^{-6}$ ), and an increase in the time to peak of the thrombin concentration (TTP;  $P = 0,0012$ ). Decreased velocity of thrombin generation (VI;  $P = 10^{-8}$ ) was the most statistically relevant indicator. Administration of antiplatelet agents had no effect on thrombograms of thrombin generation tests performed in platelet-poor plasma. Conclusion: Thrombin generation tests in platelet-rich plasma can be used to evaluate the effect of dual antiplatelet therapy. The most relevant indicator is velocity of thrombin generation.

**KEYWORDS:** thrombin generation test, antiplatelet agents, coronary heart disease, percutaneous coronary intervention

## **APIXABAN IN PATIENTS WITH ATRIAL FIBRILLATION**

**Shakhmatova O.O., Panchenko E. P.**

Institute of Clinical Cardiology named after A.L. Myasnikov, Russian Cardiology Research and Production Complex, MH RF

**C**ardiovascular disease is the most common pathology in Russia. Over 50% of deaths are caused by cardiovascular diseases, a significant proportion of which is associated with systemic thromboembolism and stroke. Atrial fibrillation significantly increases the incidence of thrombotic events for the prophylaxis of which anticoagulants are recommended. New oral anticoagulants (NOAC) have been increasingly used recently, the administration of

which does not require international normalized ratio control. The article tells about apixaban — the NOAC for the treatment of patients with atrial fibrillation.

**KEYWORDS:** atrial fibrillation, new oral anticoagulants, stroke, systemic thromboembolism, apixaban

**PREVENTION OF RECURRENT ISCHEMIC EVENTS IN PATIENTS AFTER MYOCARDIAL INFARCTION. NEW OPTIONS FOR LONG-TERM DUAL ANTIPLATELET THERAPY. RESULTS OF THE PEGASUS-TIMI54 STUDY.**

**Averkov O.V.**

Peoples' Friendship University of Russia and City Hospital #15 named after O.M. Filatov, Moscow

Cardiovascular diseases account for more than half of all deaths in Russia. Among those, coronary heart disease and myocardial infarction are the most challenging and associated with high mortality. Special attention is required to the management of patients throughout a year after myocardial infarction. During that period, the probability of recurrence of other ischemic events or cardiac death is particularly high, the fact justifying the combined use of two antiplatelet agents. The article tells about the efficacy of long-term enhancement of the effect of acetylsalicylic acid by ticagrelor in secondary prevention of ischemic events in patients after MI (according the PEGASUS-TIMI 54 study).

**KEYWORDS:** myocardial infarction, recurrent ischemic event, dual antiplatelet therapy, acetylsalicylic acid, ticagrelor

**FAST SATURATION WITH WARFARIN IS A PREDICTOR OF EXCESSIVE HYPOCOAGULATION. ADJUSTING THE ALGORITHM FOR WARFARIN DOSAGE**

Kropacheva<sup>1</sup> E.S., Borovkov<sup>3</sup> N.N., Vavilova<sup>4</sup> T.V., Vereina<sup>5</sup> N.K., Vorobyova<sup>6</sup> N.A., Galkina<sup>2</sup> I.S., Grekhova<sup>7</sup> L.V., Grontkovskaya<sup>3</sup> A. V., Donnikov<sup>2</sup> A.E., Dobrovolskiy<sup>1</sup> A.B., Zholobova<sup>5</sup> N.I., Zagorodnikova<sup>4</sup> K.A., Zateyschikov<sup>8</sup> D.A., Zemlyanskaya<sup>1</sup> O.A., Zotova<sup>8</sup> I.V., Kolevatova<sup>7</sup> G.A., Kokh<sup>9</sup> N.V., Lavrinov<sup>6</sup> P.A., Lifshits<sup>9</sup> G.I., Maksimova<sup>2</sup> O.O., Mitroshkina<sup>1</sup> M.O.,

Panchenko<sup>1</sup> E.P., Rogozina<sup>6</sup> A.S., Sinitsyn<sup>5</sup> S.P., Slepukhina<sup>9</sup> A., Sirotkina<sup>4</sup> O.V., Titaeva<sup>1</sup> E.V., Trofimov<sup>2</sup> D.Y., Fedushina<sup>3</sup> O.G., Chulkov<sup>5</sup> V.S., Tsvetovskaya<sup>9</sup> G.A.

<sup>1</sup> Institute of Clinical Cardiology named after A.L. Myasnikov, Russian Cardiology Research and Production Complex, MH RF, Moscow.

<sup>2</sup> ZAO «NPF DNA-Technology», Moscow.

<sup>3</sup> Nizhny Novgorod State Medical Academy, Department of Hospital Therapy.

<sup>4</sup> Saint-Petersburg State Medical Academy named after I.I. Mechnikov, Department of Hospital Therapy. Course of Clinical Laboratory Diagnostics.

<sup>5</sup> Chelyabinsk State Medical Academy, Department of Internal Medicine and Endocrinology, City Department of Hemostasis Pathology, CCH#11.

<sup>6</sup> Northern Branch of Hematology Research Center, Ministry of Health and Social Development of the RF, Arkhangelsk.

<sup>7</sup> Kirov Regional Cardiology Centre, Vyatka.

<sup>8</sup> Academic Medical Center of the Department of Presidential Affairs of the RF, Moscow.

<sup>9</sup> ICBFM SB RAS, laboratory of personalized medicine, Novosibirsk.

The article tells about results of a prospective follow-up of patients receiving warfarin and evaluates the key factors determining a safe maintenance dose. It was found that achieving a first INR of  $\geq 2.0$  on day 3 and 5 after start of warfarin therapy is evidently associated with excessive anticoagulation (INR  $\geq 4.0$ ). Genotype evaluation revealed dependence of warfarin saturation rate from carriage of *CYP2C9* and *VKORC1* allelic variants. Fast achievement of anticoagulant effect in the majority of cases is shown to be related to the carriage of «unfavorable genotype» (*CYP2C9* \*2/\*2 or \*3/\*3 or 2/\*3 alleles or AA *VKORC1* allelic variant<sub>1</sub>, or concomitant carriage of two heterozygous polymorphisms *CYP2C9* and *VKORC1*). Based on the obtained results, the authors concluded that INR blood test on day 3–5 after initiation of therapy had high practical value. The performed discriminant analysis determined the clinical predictor of excessive anticoagulation due to overdose of warfarin — amiodarone therapy. The findings served as the basis for the modification of the current algorithm for warfarin dosing adjustment.

**KEYWORDS:** warfarin, dosing adjustment algorithm, predictors of excessive anticoagulation

## OPTIONS FOR MEDICATION TREATMENT OF CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

**Martynyuk T.V., Dadacheva Z.K., Chazova I.E.**

Hypertension Unit, Myasnikov Research Institute of Clinical Cardiology, Russian Cardiology Research and Production Complex, MH RF

**C**hronic thromboembolic pulmonary hypertension (CTEPH) is a unique, potentially curable form of pulmonary hypertension (PH) characterized by obliteration of elastic pulmonary arteries by organized thrombus. Increase in pulmonary vascular resistance (PVR) and pulmonary artery pressure is also associated with a progressive remodelling of the distal pulmonary vascular bed. Standard treatment for CTEPH is pulmonary thrombendarterectomy. Adequate medication therapy means lifelong intake of anticoagulants. Warfarin is the drug of first choice. Medical therapies used in the treatment of pulmonary arterial hypertension (PAH) are often considered for use in inoperable patients, or for patients who have residual PH. Prostanoids, phosphodiesterase type 5 inhibitors and endothelin receptor antagonists have been studied in a number of open studies of patients with inoperable CTEPH. In the BENEFIT study, on week 16 of treatment bosentan contributed to a significant reduction in PVR and an increase in cardiac output; however, compared with placebo, it did not improve exercise tolerance after 6-min walk test. CHEST-1 (a randomized, placebo-controlled study) demonstrated the efficacy and safety of riociguat — a representative of a new class of stimulators of soluble guanylate cyclase. In September 2014, the drug was approved for the treatment of patients with inoperable and residual CTEPH in this country.

**KEYWORDS:** pulmonary hypertension, chronic thromboembolic pulmonary hypertension, thrombendarterectomy, bosentan, prostanoids, sildenafil, riociguat.

## LONG-TERM ANTITHROMBOTIC THERAPY AT HIGH RISK OF THROMBOSIS AND BLEEDING. CLINICAL OBSERVATION

**E.P. Panchenko, A.L. Komarov, M.A. Saidova, E.V. Merkulov, E.S. Kropachyova, O.O. Shakhmatova, R.V. Kaziev**

Institute of Clinical Cardiology named after A.L. Myasnikov, Russian Cardiology Research and Production Complex, Ministry of Health of the RF

**P**atients after heart surgery require antithrombotic therapy. Long-term anticoagulation therapy is especially relevant for patients who were implanted with a cardiac device. Unfortunately, antithrombotic therapy is associated with increased incidence of hemorrhage requiring long-term follow-up of patients and adequate selection of antithrombotic therapy. The article reviews a clinical case of long-term antithrombotic therapy at high risk of thrombosis and bleeding following implantation of the Watchman Device.

**KEYWORDS:** atrial fibrillation, antithrombotic therapy, anticoagulants, implantable device, Watchman closer device

## WARFARIN PHARMACOGENETICS

**Kropacheva E.S. PhD in Med.**

Associate researcher, Laboratory of Clinical Atherothrombotic Problems, Department of Angiology, Myasnikov Research Institute of Clinical Cardiology, RCRPC, MH RF, Moscow

